WHAT IS CLAIMED IS:

1. An NO-donating compound or a pharmaceutically acceptable salt thereof, comprising an NO-releasing group and a chemical moiety being covalently attached to said NO-releasing group, such that when NO is released from the compound a residue which is a naturally occurring metabolite is formed, thereby preventing or decreasing a development of tolerance to the NO-donating compound upon repetitive administration thereof,

with the proviso that the NO-donating compound is not 1-(4-methylthiazol-5-yl)ethane-1,2-diyl dinitrate and 2-(4-methylthiazol-5-yl)ethyl nitrate.

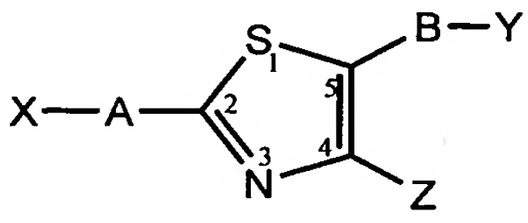
2. The NO-donating compound of claim 1, further comprising a bioactive agent residue covalently attached to said chemical moiety.

3. The NO-donating compound of claim 2, wherein said bioactive agent residue is attached to said chemical moiety via a biocleavable moiety.

4. The NO-donating compound of claim 1, wherein said naturally occurring metabolite is a thiamine metabolite.

5. The NO-donating compound of claim 4, wherein said chemical moiety comprises a substituted or unsubstituted thiazole ring.

6. The NO-donating compound of claim 5, having the general formula I:



Formula I

wherein:

A is selected from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cycloalkyl, diazo, disulfide, guanidine, guanyl,

haloalkyl, heteroalicyclic, heteroaryl, hydrazine, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, oxygen, sulfur, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, sulfur, thioalkoxy, thioaryloxy, thiocarbonyl, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a biocleavable moiety and any combination thereof, or absent;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine, guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is said NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy.

7. The NO-donating compound of claim 6, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite

residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

8. The NO-donating compound of claim 6, wherein said NO-releasing group in said Y is selected from the group consisting of a $-ONO_2$ group, a –SNO group, a diazeniumdiolate and a mesoionic oxatriazole.

9. The NO-donating compound of claim 6, wherein Z is alkyl.

10. The NO-donating compound of claim 9, wherein B is an ethylene chain.

11. The NO-donating compound of claim 9, wherein B is selected from the group consisting of $-CH_2-CH_2-O-CH_2-$, $-CH_2-CH_2-NH-CH_2-$ and $-CH_2-CH_2-S-CH_2-$.

12. The NO-donating compound of claim 10, wherein X is alkyl.

13. The NO-donating compound of claim 10, wherein X is haloalkyl.

14. The NO-donating compound of claim 10, wherein X is aryl.

15. The NO-donating compound of claim 14, wherein said aryl is selected from the group consisting of a substituted phenyl and an unsubstituted phenyl.

16. The NO-donating compound of claim 10, wherein X is heteroaryl.

17. The NO-donating compound of claim 16, wherein said heteroaryl is pyridin-3-yl.

18. The NO-donating compound of claim 10, wherein X is heteroalicyclic.

19. The NO-donating compound of claim 10, wherein X is amine.

20. The NO-donating compound of claim 10, wherein X is alkoxy.

21. The NO-donating compound of claim 10, wherein X is a moiety containing at least one NO-releasing group.

22. The NO-donating compound of claim 21, wherein said moiety is selected from the group consisting of 1-nitrooxy-ethyl, [4-methyl-5-(2-nitrooxy-ethyl)-thiazol-2-yl]-diazene, 4-methyl-5-(2-nitrooxy-ethyl)-thiazole and 2-butyl-4-methyl-5-(2-nitrooxy-ethyl)-thiazole.

23. The NO-donating compound of claim 10, wherein X is a bioactive agent residue.

24. The NO-releasing compound of claim 23, wherein said bioactive agent residue is a non-steroidal anti-inflammatory drug residue.

25. The NO-donating compound of claim 24, wherein said non-steroidal anti-inflammatory drug residue is selected from the group consisting of an aspirin residue, an ibuprofen residue and a naproxen residue.

26. The NO-donating compound of claim 23, wherein X is an anti-diabetic agent residue.

27. The NO-donating compound of claim 26, wherein said anti-diabetic agent residue is a lipoic acid residue.

28. The NO-donating compound of claim 6, wherein A is a biocleavable moiety.

29. The NO-donating compound of claim 28, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

30. The NO-donating compound of claim 28, wherein X is a bioactive agent residue.

31. The NO-donating compound of claim 28, wherein said bioactive agent residue is selected from the group consisting of a fatty acid residue, a metabolite residue, a carbohydrate residue, an amino acid residue, a peptide residue, a protein residue, a hydroxamic acid residue, a nicotinic acid residue, a nicotinamide residue, a carnitine residue, a co-enzyme residue, a beta carotene residue, a bromelain residue, a steroidal anti-inflammatory agent residue, a non-steroidal anti-inflammatory drug residue, an anti-psychotic agent residue, an anti-thrombogenic agent residue, an anti-platelet agent residue, an anti-coagulant residue, an anti-diabetic agent residue, a growth factor residue, a statin residue, a toxin residue, an antimicrobial agent residue, an analgesic residue, an anti-metabolic agent residue, a vasoactive agent residue, a vasodilator agent residue, a prostaglandin residue, a hormone residue, a thrombin inhibitor residue, an enzyme residue, an oligonucleotide residue, a nucleic acid residue, an antisense residue, a protein residue, an antibody residue, an antigen residue, a vitamin residue, an immunoglobulin residue, a cytokine residue, a cardiovascular agent residue, a chemotherapeutic agent residue, an antioxidant

residue, a phospholipid residue, an anti-proliferative agent residue, a heparin residue, and any combination thereof.

32. The NO-donating compound of claim 1, being selected from the group consisting of the compounds set forth in Table 1 and Table 2.

33. A pharmaceutical composition comprising, as an active ingredient, the NO-donating compound of claim 1 and a pharmaceutically acceptable carrier.

34. A method of treating or preventing a medical condition in which modulating an NO level is beneficial, the method comprising administering to a subject in need thereof a therapeutically effective amount of the NO-donating compound of claim 1.

35. The method of claim 34, wherein said modulating comprises elevating said NO level.

36. The method of claim 34, wherein said medical condition is selected from the group consisting of a cardiovascular disease or disorder, a gastrointestinal disease or disorder, an inflammatory disease or disorder, a respiratory disease or disorder, a central nervous system disease or disorder, a neurodegenerative disease or disorder, a psychiatric disease or disorder, a blood pressure-associated disease or disorder, a coronary artery disease or disorder, atherosclerosis, a cholesterol level-associated disease or disorder, an arterial thrombotic disease or disorder, a heart failure, a stroke, a septic shock, a NSAID-induced gastric disease or disorder, an inflammatory bowel disease or disorder, an ischemic renal disease or disorder, a peptic ulcer, diabetes, pulmonary hypertension, sickle cell anemia, asthma, a chronic obstructive pulmonary disease or disorder, dementia, epilepsy, a neuroinflammatory disease or disorder, trauma, multiple sclerosis, an erectile dysfunction, a male and female sexual dysfunction and an age-related disease or disorder.

37. The method of claim 34, further comprising administering to said subject an additional active ingredient, said additional active ingredient being capable of treating or preventing the medical condition.

38. A method of treating or preventing a medical condition in which modulating an NO level is beneficial, the method comprising administering to a subject in need thereof a therapeutically effective amount of the NO-donating compound of claim 6.

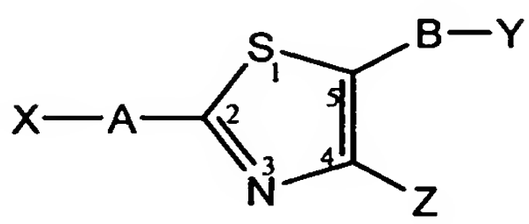
39. The method of claim 38, wherein said modulating comprises elevating said NO level.

40. The method of claim 38, wherein the medical condition is selected from the group consisting of a cardiovascular disease or disorder, a gastrointestinal disease or disorder, an inflammatory disease or disorder, a respiratory disease or disorder, a central nervous system disease or disorder, a neurodegenerative disease or disorder, a psychiatric disease or disorder, a blood pressure-associated disease or disorder, a coronary artery disease or disorder, atherosclerosis, a cholesterol level-associated disease or disorder, an arterial thrombotic disease or disorder, a heart failure, a stroke, a septic shock, a NSAID-induced gastric disease or disorder, an inflammatory bowel disease or disorder, an ischemic renal disease or disorder, a peptic ulcer, diabetes, pulmonary hypertension, sickle cell anemia, asthma, a chronic obstructive pulmonary disease or disorder, dementia, epilepsy, a neuroinflammatory disease or disorder, trauma, multiple sclerosis, an erectile dysfunction, a male and female sexual dysfunction and an age-related disease or disorder.

41. The method of claim 38, wherein said therapeutically effective amount ranges between about 0.01 mg/kg body and about 5 mg/kg body.

42. The method of claim 38, further comprising administering to said subject an additional active ingredient, said additional active ingredient being capable of treating or preventing the medical condition.

43. A method of synthesizing a compound having the general formula I:



Formula I

or a pharmaceutically acceptable salt thereof,

wherein:

A is selected from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cycloalkyl, diazo, disulfide, guanidine, guanyl, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, oxygen, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, sulfur, thioalkoxy, thioaryloxy, thiocarbonyl, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea and any combination thereof, or absent;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine, guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

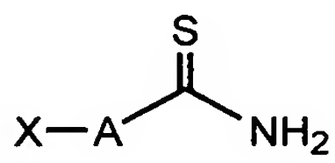
B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is an NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy;

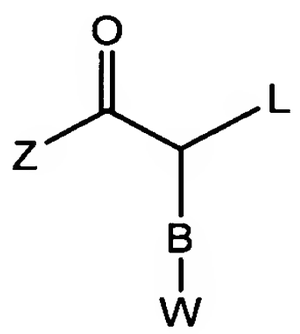
the method comprising:

providing a thioamide having a general formula II:



Formula II

providing a reactive compound having the general formula III:



Formula III

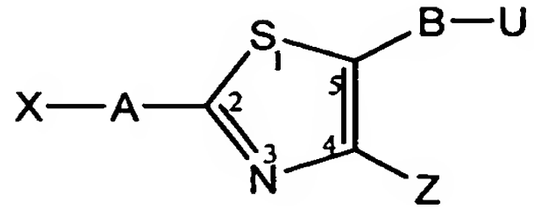
wherein:

L is a leaving group;

Z and B are as defined above; and

W is a pre-nitratable group;

reacting said thioamide having said general formula II and said compound having said general formula III, to thereby generate a thiazole derivative having a general formula IV:



Formula IV

wherein:

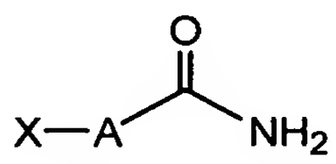
A, X, B and Z are as defined above; and

U is a nitratable group; and

converting said nitratable group into an NO-releasing group, thereby obtaining the compound having the general formula I.

44. The method of claim 43, wherein providing said thioamide comprises:

providing an amide having a general formula V:



Formula V

wherein:

X and A are as defined above; and

reacting said amide with a thiolating agent.

45. The method of claim 44, wherein said thiolating agent is phosphorous pentasulfide.

46. The method of claim 43, wherein said pre-nitratable group is selected from the group consisting of alkoxy, aryloxy, thioalkoxy, thioaryloxy, silanoxy, silicate and O-carboxylate.

47. The method of claim 43, wherein said nitratable group is selected from the group consisting of hydroxy and thiohydroxy.

48. The method of claim 43, wherein said converting comprises reacting said thiazole derivative having said formula IV with a nitrating agent, said nitrating agent containing said NO-releasing moiety.

49. The method of claim 48, wherein said NO-releasing moiety is ONO_2 and said nitrating agent is nitric acid.

50. The method of claim 47, wherein said NO-releasing moiety is ONO_2 and said nitrating agent is nitric acid.

51. The method of claim 43, wherein said leaving group is selected from the group consisting of halide, alkoxy, aryloxy, amine, hydroxy, azide, nitro, cyano, thiocyanate, O-carboxylate, thiohydroxy and sulfonate.

52. The method of claim 43, wherein said pre-nitratable group is acetate and said nitratable group is hydroxy.

53. The method of claim 43, wherein said reactive compound having said general formula III is 5-acetoxy-3-chloro-2-pentanone.

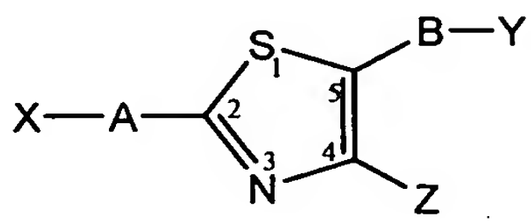
54. The method of claim 43, wherein A is a biocleavable moiety.

55. The method of claim 54, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

56. The method of claim 43, wherein X is a bioactive agent residue.

57. The method of claim 43, wherein said compound is selected from the group of compounds set forth in Table 1 and Table 2.

58. A method of synthesizing a compound having the general formula I:



Formula I

or a pharmaceutically acceptable salt thereof,

wherein:

A is a biocleavable moiety;

X is selected from the group consisting of acyl-halide, alkenyl, alkoxy, alkyl, alkynyl, amine, amine-oxide, aryl, aryloxy, azo, borate, C-amide, carbonyl, C-carboxylate, C-thiocarboxylate, cyano, cycloalkyl, diazo, disulfide, guanidine, guanyl, halide, haloalkyl, heteroalicyclic, heteroaryl, hydrazine, hydrogen, hydroxy, N-amide, N-carbamate, N-dithiocarbamate, nitro, N-sulfonamide, N-thiocarbamate, O-carbamate, O-carboxylate, O-thiocarbamate, O-thiocarboxylate, oxime, peroxo, phosphate, phosphine-oxide, phosphine-sulfide, phosphinyl, phosphite, phosphonate, pyrophosphate, S-dithiocarbamate, silaza, silicate, siloxy, silyl, S-sulfonamide, sulfate, sulfite, sulfonate, sulfoxide, thioalkoxy, thioaryloxy, thiocarbonyl, thiohydroxy, thiophosphate, thiosulfate, thiosulfite, thiourea, triphosphate, urea, a bioactive agent residue, a moiety containing at least one NO-releasing group, a substituted or unsubstituted thiazole and any combination thereof;

B is selected from the group consisting of a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms, and a saturated or unsaturated, substituted or unsubstituted alkylene chain having 1-20 carbon atoms interrupted by at least one heteroatom, whereby said at least one

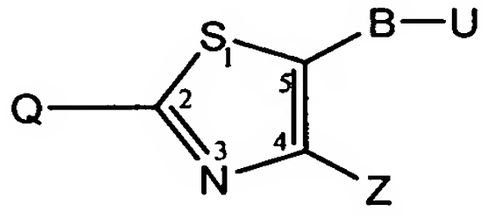
heteroatom comprises oxygen, sulfur, nitrogen, phosphor, silicon and any combination thereof;

Y is an NO-releasing group; and

Z is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, amine, cycloalkyl, heteroalicyclic, aryl, heteroaryl, halide, haloalkyl, hydroxy, thiohydroxy, alkoxy, thioalkoxy, aryloxy and thioaryloxy;

the method comprising:

providing a thiazole having a general formula VI:



Formula VI

wherein:

Z, B and U are as defined above; and

Q is a first reactive group;

providing a compound the general formula VII:

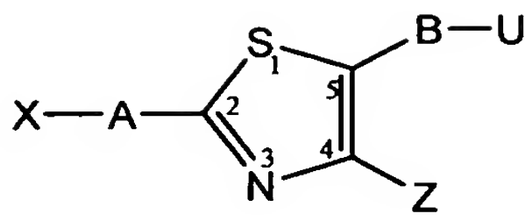
Formula VII

wherein:

X is as defined above; and

K is a second reactive group;

reacting said thiazole having said general Formula VI and said compound having said general Formula VII, to thereby generate a thiazole derivative having a general Formula IV:



Formula IV

wherein:

A, X, B and Z are as defined above; and

U is a nitratable group; and

converting said nitratable group into an NO-releasing group, thereby obtaining the compound having the general Formula I.

59. The method of claim 58, wherein said biocleavable moiety is selected from the group consisting of amide, carboxylate, carbonate, carbamate, phosphate, hydrazide, thiohydrazide, disulfide, epoxide, peroxo and methyleneamine.

60. The method of claim 58, wherein each of said first reactive group and said second reactive group is independently selected from the group consisting of amine, halide, acyl-halide, sulfonate, sulfoxides, phosphate, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, cyano, nitro, azo, isocyanate, sulfonamide, C-carboxylate, O-carboxylate, N-thiocarbamate, O-thiocarbamate, urea, thiourea, O-carbamate, N-carbamate, C-amide, N-amide, guanyl, guanidine and hydrazine.

61. The method of claim 58, wherein said nitratable group is selected from the group consisting of hydroxy and thiohydroxy.

62. The method of claim 58, wherein said converting comprises reacting said thiazole derivative having said Formula IV with a nitrating agent, said nitrating agent containing said NO-releasing moiety.

63. The method of claim 62, wherein said NO-releasing moiety is ONO_2 and said nitrating agent is nitric acid.

64. The method of claim 58, wherein X is a bioactive agent residue.

65. A medical device comprising the NO-donating compound of claim 1 and a delivery system configured for delivering said NO-donating compound to a bodily site of a subject.

66. The medical device of claim 65, wherein said NO-donating compound forms a part of a pharmaceutical composition, said pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

67. The medical device of claim 65, wherein said delivering is effected by inhalation.

68. The medical device of claim 67, wherein said delivery system is selected from the group consisting of a metered dose inhaler, a respirator, a nebulizer inhaler, a dry powder inhaler, an electric warmer, a vaporizer, an atomizer and an aerosol generator.

69. The medical device of claim 65, wherein said delivering is effected transdermally.

70. The medical device of claim 69, wherein said delivery system is selected from the group consisting of an adhesive plaster and a skin patch.

71. The medical device of claim 65, wherein said delivering is effected topically.

72. The medical device of claim 71, wherein said delivery system is selected from the group consisting of an adhesive strip, a bandage, an adhesive plaster, a wound dressing and a skin patch.

73. The medical device of claim 65, wherein said delivering is effected by implanting the medical device in a bodily organ.

74. The medical device of claim 73, wherein said delivery system is selected from the group consisting of an aortic aneurysm graft device, an atrioventricular shunt, a catheter, a defibrilator, a heart valve, a hemodialysis catheter, a hemodialysis graft, an indwelling arterial catheter, an indwelling venous catheter, a needle, a pacemaker, a pacemaker lead, a patent foramen ovale septal closure device, a stent, a stent graft, a suture, a synthetic vascular graft, a thread, a tube, a vascular anastomosis clip, a vascular aneurysm occluder, a vascular clip, a vascular prosthetic filter, a vascular sheath and a drug delivery port, a venous valve and a wire.

75. The medical device of claim 73, wherein said organ is selected from the group consisting of a pulmonary cavity, a blood vessel, an artery, a vein, a capillary, a heart, a heart cavity and a visceral organ.